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Citation for final published version:

Armstrong, Robert David, Hirayama, Jun, Knight, David W and Hutchings, Graham J. ORCID: <https://orcid.org/0000-0001-8885-1560> 2019. Quantitative determination of Pt- catalyzed D-glucose oxidation products using 2D NMR. ACS Catalysis 9 (1) , pp. 325-335. 10.1021/acscatal.8b03838 file

Publishers page: <http://dx.doi.org/10.1021/acscatal.8b03838>
<<http://dx.doi.org/10.1021/acscatal.8b03838>>

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Quantitative Determination of Pt-Catalyzed D-Glucose Oxidation Products Using 2D NMR

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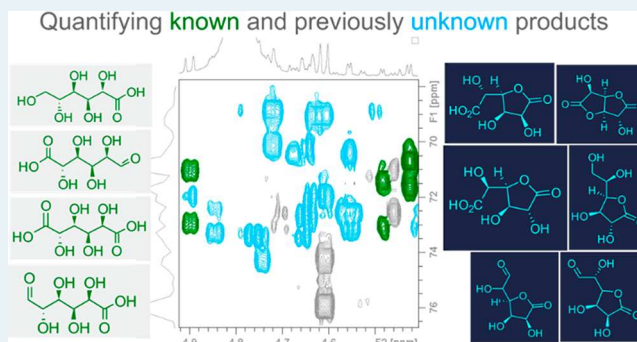
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Supporting Information

ABSTRACT: Quantitative correlative ¹H–¹³C NMR has long been discussed as a potential method for quantifying the components of complex reaction mixtures. Here, we show that quantitative HMBC NMR can be applied to understand the complexity of the catalytic oxidation of glucose to glucaric acid, which is a promising bio-derived precursor to adipic acid, under aqueous aerobic conditions. It is shown through 2D NMR analysis that the product streams of this increasingly studied reaction contain lactone and dilactone derivatives of acid products, including glucaric acid, which are not observable/quantifiable using traditional chromatographic techniques. At 98% glucose conversion, total C₆ lactone yield reaches 44%. Furthermore, a study of catalyst stability shows that all Pt catalysts undergo product-mediated chemical leaching. Through catalyst development studies, it is shown that sequestration of leached Pt can be achieved through use of carbon supports.

KEYWORDS: partial oxidation, quantitative 2D NMR, glucose, glucaric acid, gluconic acid, carbohydrates



1. INTRODUCTION

Combined environmental, economic, and political pressures are incentivizing the drop-in integration of bio-derived, sustainable feedstocks within the chemical industry. As a highly abundant C₆ monosaccharide, the selective oxidation of glucose has received significant attention in recent years. In particular, research has focused upon the selective oxidation of glucose to gluconic acid, which is used in the food, pharmaceutical, and paper industries. A number of heterogeneous, precious metal catalysts have been reported to catalyze this reaction using molecular oxygen as the oxidant. These often comprise Pt, Pd, and Au^{1–6} and might also contain promoters such as Bi.^{2,7–9} Less extensively studied is the selective oxidation of glucose to glucaric acid, an aldaric acid which was recently recognized by the U.S. Department of Energy as a key bio-derived platform molecule.¹⁰

Glucaric acid is produced industrially through oxidation of glucose with nitric acid, a process which dates back to 1888 and affords ca. 40% yield of the monopotassium salt.^{11–13} Byproducts for this reaction include oxalic, tartaric, and 5-ketogluconic acid.¹² With potential applications in the food, pharmaceutical, and polymer industries, global demand for glucaric acid is predicted to increase through the 21st century.^{14–21} Processes for the enzymatic, electrocatalytic, and heterogeneously catalyzed synthesis of glucaric acid from glucose have also been reported.^{19,20,22–33} The TEMPO-promoted oxidation of glucose to glucaric acid (>90% yield), with NaBr, bleach, and strict pH control has also been

reported;³⁴ however, these reactions generate toxic byproducts. Of the many approaches taken, the heterogeneously catalyzed systems utilizing molecular oxygen present the most atom efficient, inherently green approach to glucaric acid production. Studies into heterogeneously catalyzed oxidation processes typically fall into two categories: (i) pH-controlled^{6,27,32,35} and (ii) non-pH-controlled.^{21,29–31,33} Dirckx et al.²⁷ reported that strict control of pH at 9–10 enhances the activity of Pt catalysts, which was attributed to more rapid desorption of free-acid products from the active site. Meanwhile Rennovia Inc. recently claimed glucaric acid yields of 66% in the absence of pH control, over a range of monometallic Pt and bimetallic AuPt catalysts.^{20,29,30} To date, however, studies have failed to address either spectroscopic analysis of product streams or the long-term stability of catalysts operating under autogenous pH. The latter is particularly pertinent as products of glucose oxidation, gluconic, glucaric, and tartaric acids, are known metal-sequestering agents.^{27,36} Indeed, Karski et al. reported leaching of M (M = Bi, Tl, Sn, and Co) and low levels of Pd when bimetallic Pd-M/carbon and silica catalysts were used to catalyze the oxidation of glucose to gluconic acid.³⁷ This was attributed to the strong chelating properties of gluconic acid.³⁷

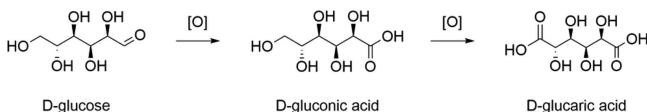
Received: September 24, 2018

Revised: November 23, 2018

Published: November 30, 2018

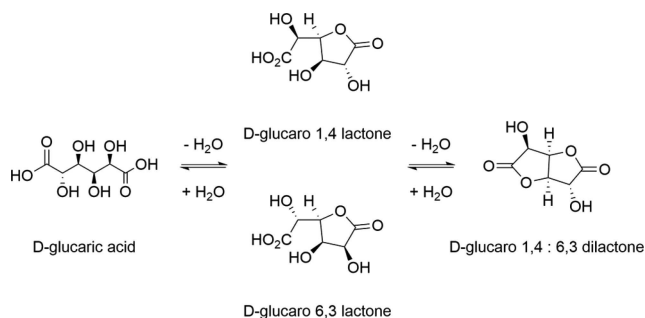
Chromatographic techniques are favored for separation and quantification of the products of glucose oxidation, and C₆ products are accepted to form according to the pathways shown in Scheme 1.^{19–21,27,29–33,35,38,39} Glucaric acid is

Scheme 1. Oxidative Conversion of Glucose to Glucaric Acid



generally accepted to be the terminal C₆ oxidation product, with lower molecular weight carboxylic acids formed through undesirable C–C scission pathways. However, juxtaposed with high reported mass balances in catalysis studies are equilibria known to establish between D-glucaric acid and its mono- and di-lactone derivatives: D-glucaro-1,4-lactone, D-glucaro-6,3-lactone and D-glucaro-1,4:6,3-dilactone under acidic conditions (Scheme 2).⁴⁰ While never reported as quantified products of

Scheme 2. Equilibration of D-Glucaric Acid with Its Mono- and Dilactone Derivatives



glucose oxidation, Boussie et al. implied that these derivatives might form *in situ* under their reaction conditions.²⁰ Meanwhile, reported short chain acid byproducts of Pt-catalyzed aerobic glucose oxidation include tartronic acid, tartaric acid, oxalic acid, formic acid, glycolic acid, and glyceric acid.

Of the analytical techniques available, nuclear magnetic resonance (NMR) is among the most versatile, with the potential for simultaneous quantification of multiple small organic molecule components within a complex mixture.^{41,42} Two dimensional NMR, in particular heteronuclear multiple-bond correlation (HMBC) spectroscopy, exemplifies this due to its ability to separate overlapping ¹H resonances. However, a key drawback with 2D techniques is that the intensity of a 2D NMR correlation is molecule and environment dependent, leading to difficulty in determining absolute concentrations. While it has been shown that this can be mitigated to some degree through addition of a standard,⁴² the correlations representative of the standard molecule also suffer environmental effects, leading to nonlinear calibrations.⁴²

In the current study, aerobic oxidation of glucose over supported Pt catalysts is studied under autogenous pH. Both C₆ products and glucose conversion are quantified using quantitative ¹³C–¹H HMBC NMR. It is shown that the mono- and dilactone derivatives of D-glucaric acid featured in Scheme 2 form *in situ* and at appreciable selectivities, as do D-glucuronic and L-guluronic acids, the derived five-membered lactones thereof and also carbon dioxide. Elemental analyses of

product streams show that heterogeneous Pt catalysts undergo product-mediated chemical leaching. This non-transient leaching increases with glucose conversion, with leaching levels of up to 24% of total supported Pt observed. It is shown that by supporting Pt on a carbon support, or addition of carbon, leached Pt can be effectively sequestered to yield a product stream which is effectively platinum-free. At 98% D-glucose conversion, a catalyst comprising 5 wt % Pt/C prepared by wet impregnation afforded 59% yield of D-glucaric acid and its lactone derivatives, a mass balance of 93%, and a low Pt-concentration of 1.4 ppm.

2. RESULTS AND DISCUSSION

2.1. Product Identification by NMR. To date, all studies relating to catalytic D-glucose oxidation have utilized chromatographic (HPLC/IC) techniques for quantification of reaction products, substrate conversion, and identifying products based on retention times. Indeed, these techniques are favored for such processes, owing to the availability of a wide range of stationary phases for the separation of low molecular weight organic acids. Our previous studies into the preparation of crystalline D-glucaric acid showed its rapid lactonization to occur at mild temperatures (<50 °C), despite being in an aqueous environment.⁴³ Indeed, the pathways shown in Scheme 2 have previously been studied using ¹H NMR.⁴⁰ However, while alluded to within the patent literature,^{30,38,44} no study has as yet reported formation of lactone or dilactone derivatives of D-glucaric acid under catalytic conditions, let alone sought to quantify these potential reaction products. Similarly, often overlooked are D-glucuronic and L-guluronic acids, both glucose-derived uronic acids which have been reported to undergo oxidation to yield glucaric acid.^{27,45} In line with previous studies, these molecules and other potential C₆ products of D-glucose oxidation were analyzed via HPLC using an acid-specific stationary phase (Agilent, Metacarb 67H; Supporting Information Figure S1). Despite method optimization, significant overlapping of peaks was observed in both RID and DAD (210 nm) signals. Indeed, it was apparent that separation of D-glucurono, L-gulurono, D-glucano, and D-glucaro products was not feasible, as shown in Figure S1.

To determine which C₆ products form under glucose oxidation conditions, 5 wt % Pt on TiO₂ (P25) was prepared by wet impregnation (5 wt % Pt/TiO₂^{IMPre400}). This catalyst was assessed in D₂O under the following reaction conditions: 40 mg catalyst, 1000 rpm, P(O₂) = 20 bar, 80 °C, 24 h, [D-glucose] = 0.554 M, 5.54 mmol (D-glucose/Pt = 540:1 mol/mol). The ¹H NMR spectrum of aqueous products (Supporting Information Figure S2) showed multiple overlapping resonances within the δ 3.0 ppm to δ 5.6 ppm region, with a strong solvent resonance centered at δ 4.79 ppm attributable to H₂O. Objective assignment of ¹H resonances in Supporting Information Figure S2 was not possible; therefore 2D HMBC NMR was employed, with an aim to separate ¹H environments along the ¹³C axis. The ¹³C–¹H HMBC spectra are shown in Figure S3, with correlations assigned through analysis of commercial standards where possible (alternately, synthesized standards), and chemical structures are shown in Table S1, with ¹³C–¹H assignments shown in Table S2. An expanded region of this spectrum is shown in Figure 1, with spectral features assigned through false coloring based on analysis of standards. It is clear from Figure 1 that Pt-catalyzed aerobic oxidation of glucose under autogenous pH affords a far

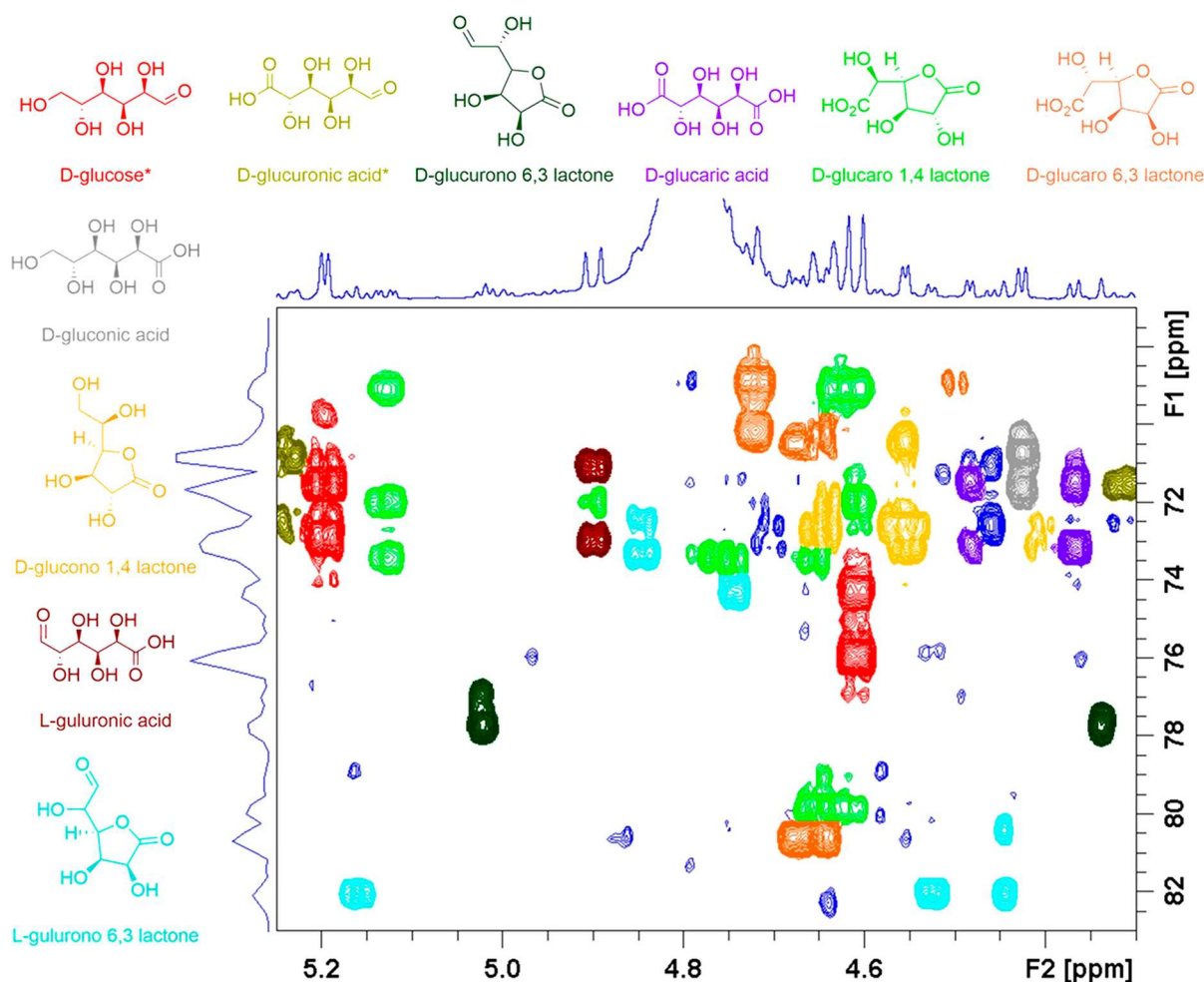
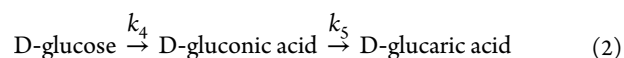
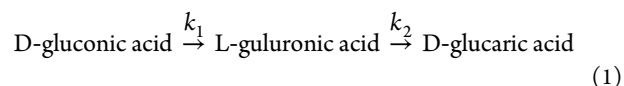


Figure 1. Expanded region of a false-colored ^{13}C – ^1H HMBC-NMR spectrum of the product stream from D-glucose oxidation catalyzed by 5 wt % Pt/TiO₂^{IMPRed400} with O₂. The structures of C₆ gluconic, glucuronic, guluronic, and glucaric acids and their derivative products are shown. F1 axis is the ^{13}C spectrum; F2 is the ^1H spectrum (dark blue ■, unassigned). *D-glucose and D-glucuronic acid present in solution as α/β cyclic anomers. Conditions: 5% Pt/TiO₂^{IMPRed400} (40 mg), [D-glucose] = 0.554 M (5.54 mmol in D₂O), 80 °C, 1000 rpm, $P(\text{O}_2)$ = 20 bar, 24 h.

more complex mixture of C₆ oxidation products than shown in Scheme 1. Indeed, ^{13}C – ^1H correlations consistent with three uronic acids: D-glucuronic acid, D-gluconic acid, and L-guluronic acid are observed. Lactone derivatives of these, D-glucurono-6,3-lactone, D-glucono-1,4-lactone, and L-gulurono-6,3-lactone, were also observed, with integrated peak areas suggesting that these form in significant concentrations. D-Glucaro-1,4-lactone and D-glucaro-6,3-lactone are also confirmed, for the first time, to be products of D-glucose oxidation under aqueous conditions. Potential pathways to formation of these C₆ products are shown in Scheme 3. 5-Keto-D-gluconic acid and the hemiacetal forms of D-fructose, α -D-fructofuranose/ α -D-fructopyranose, however, were not observed as reaction products. No dialdehyde products were observed. Meanwhile, studies on commercial standards of D-glucono-1,5-lactone (10) showed it to undergo spontaneous conversion (STP) to D-gluconic acid (8). This was characterized by a shift in δ ^{13}C from 173.8 to 175.9 ppm and decreased intensity of correlations at δ ^{13}C = 81.6 ppm. The thermodynamic instability of six-membered D-glucono-1,5-lactone (10) relative to five-membered D-glucono-1,4-lactone (9) is consistent with previous studies.⁴⁶

To confirm the C₆ pathways proposed in Scheme 3, the three uronic acid products identified in Figure 1, D-glucuronic

acid (4), D-gluconic acid (8), and L-guluronic acid (11), were treated under oxidation conditions in the presence of 5% Pt/TiO₂^{IMPRed400}. Conversion of the target aldaric acid, D-glucaric acid (13), was also assessed under the same conditions, and HMBC NMR spectra of product streams are shown in Table S3, entries 1–4. These studies confirmed that the three uronic acids undergo oxidation to yield D-glucaric acid (13). An equilibrium with D-glucaro-1,4-lactone (14) and D-glucaro-6,3-lactone (15) is then established. Dehydrogenation of D-gluconic acid (8) was observed, yielding L-guluronic acid (11) and L-gulurono-6,3-lactone (12; Table S3, entry 1), with D-glucono-1,4-lactone (9) also observed. This was found to be consistent with previous work by Dirx et al., who reported that for eq 1, $k_1 \ll k_2$.²⁷



Recently, Lee et al. identified dehydrogenation of D-gluconic acid as a potential rate limiting step in the formation of D-glucaric acid from glucose, though they reported no formation of L-guluronic acid or any derivatives.³³ Indeed, Scheme 1 and

(5) a-D-glucuronic acid **(6) D-glucuro 6,3 lactone** **(7) β-D-glucuronic acid** **(14) D-glucaro 1,4 lactone**

(2) a-D-glucopyranose **(4) D-glucuronic acid** **(13) D-glucaric acid** **(16) D-glucaro 1,4 : 6,3 dilactone**

(3) β-D-glucopyranose **(1) D-glucose** **(11) L-guluronic acid** **(15) D-glucaro 6,3 lactone**

(9) D-glucano 1,4 lactone **(8) D-gluconic acid** **(10) D-glucono 1,5 lactone** **(12) L-gulurono 6,3 lactone**

interaction of reaction products with the NMR standard itself, a melt-sealed glass ampule containing 1 wt % TMS/ CDCl_3 was used as an internal standard in calibrations and product analyses. Two different methods were then used in calibrating for glucose oxidation reaction products using HMBC NMR. These were (i) linear calibrations using commercially available standards and (ii) calibration through equilibrium studies. Approach ii was adopted in calibration of molecules which could be neither purchased nor isolated in pure, quantifiable crystalline form but rather exist as equilibrium mixtures. These include (a) α -D-glucopyranose (**2**) \rightleftharpoons β -D-glucopyranose (**3**), the aqueous forms of D-glucose (**1**), (b) α -D-glucuronic acid (**5**) \rightleftharpoons β -D-glucuronic acid (**7**) and (c) D-glucaro-6,3-lactone (**15**), which was cross-calibrated via the equilibria shown in [Scheme 2](#) using rF's derived for D-glucaric acid (**13**), D-glucaro-1,4-lactone (**14**), and D-glucaro-1,4:6,3-dilactone (**16**). For a range of concentrations (in D_2O), each characteristic ^1H – ^{13}C correlation was normalized to the TMS standard at δ ^1H = 0 ppm and δ ^{13}C = 0 ppm to afford a response factor (rF). Sensitivity analyses were then carried out for the rF's of each ^1H – ^{13}C correlation within a specific HMBC spectrum of a product using model reaction solutions. In this way, those correlations were identified which were least susceptible to drift from their linear calibrations when present in complex product streams. In addition to sensitivity analyses, only distinct, non-overlapping peaks were considered for quantitative analyses. An example of route i depicting calibration of D-glucaric acid (**13**) is shown in [Figure S4](#) and [Tables S5 and S6](#), while calibration of D-glucaro-6,3-lactone (**15**) via route ii is shown in [Figures S5 and S6](#) and [Tables S7–S9](#). A truly quantitative, standardized first order NMR method for determining the concentration of D-glucose (as α - and β -D-

Table 1. Aqueous Aerobic Oxidation of Glucose over Various Supported 5 wt % Pt Catalysts, Catalytic Activity and Stability^{a,b}

entry	cat	$\chi/\%$ ^c	product selectivities/% ^d												C _{bal} /%	[M] ppm ^g
			GLU	GLU _{1,4}	GLA	GL _{1,4}	GL _{6,3}	GL _{1,4;6,3}	GLUU ^e	GLUU _{6,3}	GUL	GUL _{6,3}	other ^f	CO ₂		
1	none	0													101	
2	TiO ₂	0													99	
3	SiO ₂	0													101	
4	C (XC72R)	0													101	
5	Pt/TiO ₂ ^{IWI}	42.2	14.8	11.4	8.5	1.7	9.1	0.6	11.1	10.6	15.6	11.0	5.2	0.4	100	6.8
6	Pt/TiO ₂ ^{CVI}	55.5	22.7	18.6	5.7	2.0	7.5	0.5	4.0	5.1	13.8	12.5	6.0	1.6	95	7.0
7	Pt/TiO ₂ ^{IMP}	49.0	17.9	16.6	6.7	1.7	6.0	0.4	6.1	7.6	14.2	13.2	5.7	3.9	97	7.9
8	Pt/SiO ₂ ^{IWI}	26.0	19.3	16.4	4.5	1.6	5.2	0.8	10.4	11.6	14.4	13.5	1.7	0.6	102	2.0
9	Pt/SiO ₂ ^{CVI}	76.9	2.9	1.5	11.5	3.0	8.0	1.0	11.6	17.0	15.8	10.3	13.5	3.9	74	12.6
10	Pt/SiO ₂ ^{IMP}	16.2	34.3	26.1	0.0	2.9	1.0	0.0	6.7	5.2	9.2	9.7	3.6	1.2	96	1.1
11	Pt/C ^{IMP}	44.3	32.2	27.2	4.6	1.2	5.4	0.2	3.1	4.1	11.0	8.3	2.3	0.4	102	1.0
12	Pt/C ^{IWI}	57.8	24.8	22.8	6.5	2.1	5.8	0.7	4.4	5.2	12.1	10.8	3.9	0.8	102	1.0
13	Pt/C ^{CVI}	56.9	25.5	22.0	5.9	1.8	6.6	0.4	4.0	4.2	13.6	10.2	4.6	1.2	95	1.0

^aGLU (D-glucuronic acid), GLU_{1,4} (D-glucurono-1,4-lactone), GLA (D-glucaric acid), GL_{1,4} (D-glucaro-1,4-lactone), GL_{6,3} (D-glucaro-6,3-lactone), GL_{1,4;6,3} (D-glucaro-1,4:6,3-dilactone), GLUU (D-glucuronic acid), GLUU_{6,3} (D-glucurono-6,3-lactone), GUL (L-guluronic acid), GUL_{6,3} (L-gulurono 6,3-lactone). ^bConditions; 40 mg catalyst, [D-glucose] = 0.554 M (5.54 mmol in D₂O), 80 °C, 1000 rpm, P(20% O₂/N₂) = 25 bar, 24 h, glucose/Pt (mol/mol) = nominal 540:1 where applicable. ^cGlucose conversion quantified from disappearance of glucose (α and β glucopyranose) using HMBC NMR. ^dBased on observed reaction products. ^eQuantified as α - and β -D-glucuronic acid. ^fOther (tartaric acid, tartronic acid, glycolic acid, glyceric acid, oxalic acid, acetic acid). ^gDetermined by MPAES (note: where applicable, 100% Pt leaching would afford a [Pt] of 200 ppm).

glucopyranose) in solution was employed (Figure S7), with validation of rF's shown in Figure S8. A representative sensitivity analysis is shown in Table S6. Such an analysis was carried out for all derivatives shown in Table S1, with the exception of D-glucaro-6,3-lactone and α/β -D-glucuronic acid—for which pure standards were unavailable. For these, nonoverlapping correlations (where $R^2 > 0.99$) were used in quantification. The ¹H–¹³C correlations used in quantifying unreacted glucose and oxidation products are shown in Table S10. ¹³C–¹H HSQC NMR was also considered for use in product stream analysis due to its being a more sensitive technique and less susceptible to variation in ¹³C–¹H couplings. However, observed ¹³C–¹H correlations were too intense for objective TMS-normalized quantitative analysis of product streams without product stream dilution (Figure S9), which could shift the position of the dynamic equilibria shown in Scheme 3.

To further validate the applicability of quantitative ¹³C–¹H HMBC NMR in these systems, 5% Au/TiO₂^{IMPRed400} was prepared and assessed for non pH-controlled D-glucose oxidation, a reaction which is broadly reported to yield D-glucuronic acid (8) as the terminal C₆ product. Two C₆ products were observed in HMBC NMR spectra of reaction solutions across 20 h on-line, D-glucuronic acid (8) and D-glucurono-1,4-lactone (9). As was shown in Figure S1, these products are separable via HPLC. Comparative quantitative analyses of product streams at 2–20 h on line via HMBC NMR and HPLC are shown in Figure S10. Ring-opening of the lactone was observed during calibration and is attributed to the polar mobile and strongly cationic stationary phase within the HPLC column. This was characterized by a consistently lower lactone/ acid ratio observed in HPLC relative to HMBC NMR data (Figure S10a and b, respectively). Nonetheless, the Σ yield of D-glucuronic acid derivatives (D-glucuronic acid + D-glucurono-1,4-lactone) was consistent between analytical techniques (Figure S10c).

To discount any potential effects from the use of D₂O as a solvent, 5% Pt/TiO₂^{IMPRed400} was also assessed in deionized H₂O. A comparison of HMBC NMR spectra for reactions

carried out in either D₂O or H₂O can be found in Figure S11. While the same distribution of products formed as in Figure 1, spectral resolution is significantly obscured by the presence of a strong solvent resonance centered at *ca.* δ ¹H = 4.9 ppm (± 0.25 ppm), with certain characteristic ¹H–¹³C interactions effectively obscured. These are indicated in Figure S11a. Analysis of the product streams from Figure S11 using ²H NMR indicated that no deuterium exchange occurred during catalytic assessments (Figure S12). All reactions and calibrations were therefore carried out in D₂O to allow for accurate quantification of products. In addition, and for the first time, CO₂ is quantified as a product of Pt-catalyzed D-glucose oxidation, as determined through GC-FID analysis of gaseous product streams.

2.3. Assessment of Supported Pt Catalysts in the Aerobic Oxidation of D-Glucose. Blank reactions were carried out in the absence of a catalyst (Table 1, entry 1) and also in the presence of unmodified support materials P25 TiO₂, SiO₂, and carbon (Table 1, entries 2, 3, and 4, respectively). No glucose conversion was observed in the presence of these unmodified support materials. For these experiments, the carbon mass balance at *t* = 24 h was 100% \pm 1%, with glucose quantified post-reaction (as α and β glucopyranose) using HMBC NMR. Direct quantification of glucose conversion in this way is a key distinction between the reported quantitative NMR technique and chromatographic methodologies, which suffer from coelution of products and substrate. Consistent with previous reports on the oxidation of D-glucose to D-glucaric acid, a range of catalysts containing a nominal 5 wt % loading of Pt supported on SiO₂ (Divasil 635), TiO₂ (Degussa, P25), and carbon (Vulcan, XC72R) were prepared via IMP, IWI, and CVI, this being a representative sample of preparation methodologies, support materials, and Pt precursors. To allow for comparison of catalysts, assessments were carried out at <100% conversion: [D-glucose] = 0.554 M, 24 h, 80 °C, P(20% O₂/N₂) = 25 bar. Through quantitative HMBC analysis of product streams shown in Table 1, six additional C₆ products of Pt-catalyzed D-glucose oxidation are now reported for the first time (Table 1, entries 5–13). These are D-glucurono-

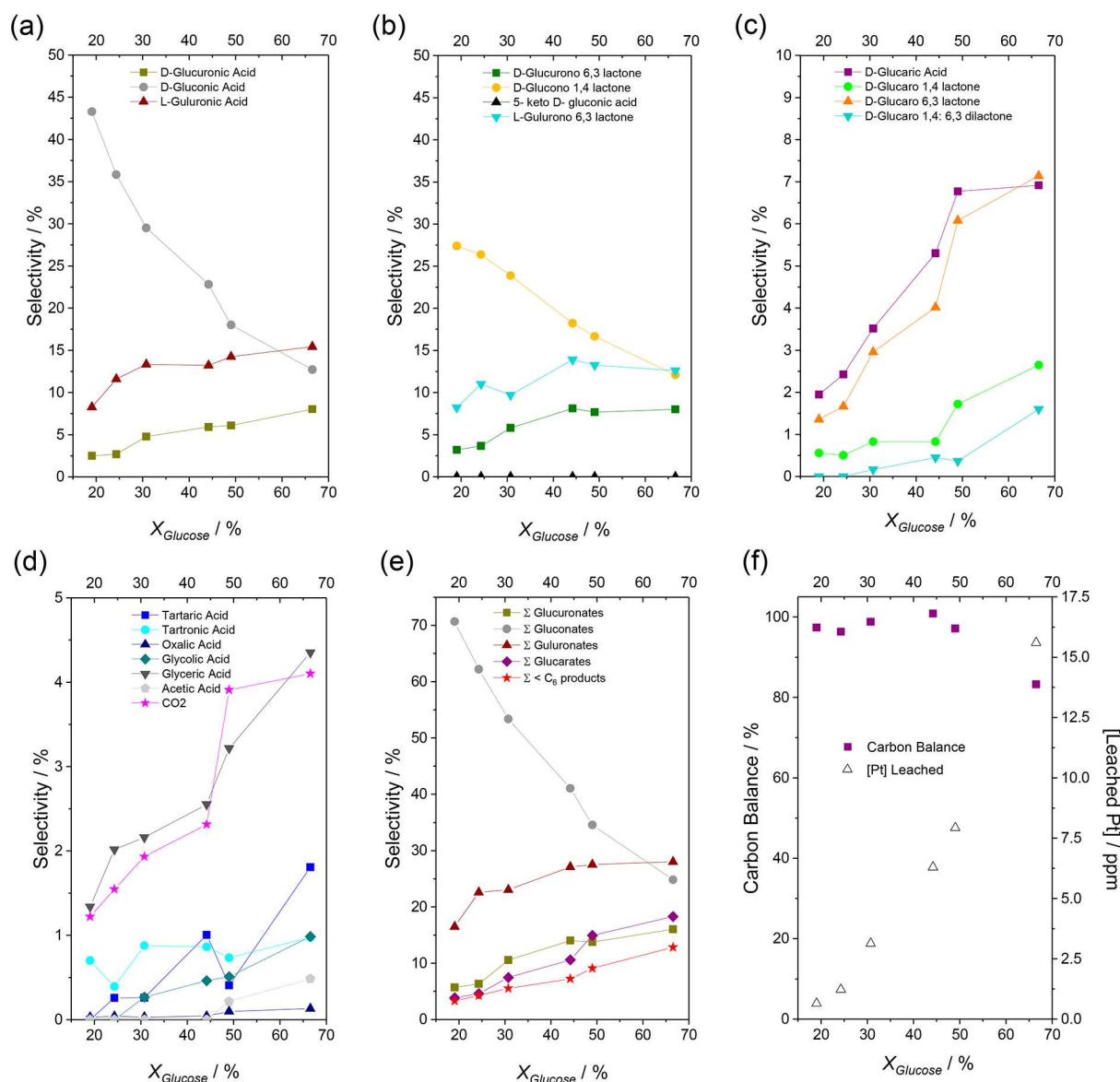


Figure 2. Temporal evolution of products in aerobic D-glucose oxidation catalyzed by 5% Pt/TiO₂^{IMPreD400} showing glucose conversion (X_{Glucose}), selectivities toward (a) uronic acid products, (b) lactone derivatives of uronic acid products, (c) glucarate products, and (d) $< C_6$ products. Also showing (e) Σ selectivities toward product groups and (f) carbon mass balances + Pt leaching. Conditions: 5% Pt/TiO₂^{IMPreD400} (40 mg), [D-glucose] = 0.554 M (5.54 mmol in D₂O), 80 °C, 1000 rpm, P(20% O₂/N₂) = 25 bar.

1,4-lactone (GLU_{1,4}; **9**), D-glucaro-1,4-lactone (GL_{1,4}; **14**), D-glucaro-6,3-lactone (GL_{6,3}; **15**), D-glucaro-1,4:6,3-dilactone (GL_{1,4:6,3}; **16**), D-glucurono-6,3-lactone (GLU_{6,3}; **6**), and L-gulurono-6,3-lactone (GUL_{6,3}; **12**). Total oxidation to CO₂ was also assessed, with yields of up to 2.0% determined (Table 1, entry 7). In the presence of Pt catalysts, low glucose conversion correlated with high selectivity toward D-gluconic acid and its derivatives (Table 1, entry 10). With increasing conversion, selectivity toward derivatives of D-glucaric (**13**, **14**, **15**, **16**) and L-guluronic acid (**11**, **12**) increases. At near isoconversion, comparable product selectivities were observed for Pt/TiO₂^{CVI}, 5% Pt/C^{CVI}, and 5% Pt/C^{IWI} (Table 1, entries 6, 12, and 13), despite the significant disparity in BET surface areas of the TiO₂ and carbon supports (48 and 226 m² g⁻¹, respectively). Indeed, the physicochemical property which best correlated with observed D-glucose conversion rates was Pt surface area, as determined by CO pulse titration (Figure S13a). ICP-MS analysis of the product streams also showed

leaching of Pt into solution. This was determined to be product-mediated, with leaching observed only when the reactor was charged with both the O₂ and D-glucose (Table S11). At isoconversion, lower [Pt] concentrations were observed for entries 12 and 13 than for entry 7, and this can be attributed to the ability of carbon to effectively sequester leached Pt from aqueous solution, as confirmed by studies shown in Figure S14. To determine whether the observed product-mediated leaching of Pt was a transient phenomenon, 5% Pt/TiO₂^{IMPreD400} was assessed under continuous flow conditions in a trickle flow regime (Figure S15a). Pt leaching was observed to continue at steady state over 40 h on stream, in line with steady state glucose conversion. Consistent with batch reaction studies in Table 1, it is shown in Figure S15b that through addition of carbon extrudates (Norit ROW Supra, Sigma-Aldrich) after the Pt-catalyst bed, leached Pt can be effectively sequestered from the product stream onto the carbon. It is perhaps serendipitous, therefore, that Rennovia

Table 2. A Parametric Study of 5% Pt/TiO₂^{IMPRed400} and 5% Pt/C^{IMPRed400} Catalyzed D-Glucose Oxidation^{a,b}

entry	conditions; % O ₂ / temp °C/mg cat	χ/% ^c	observed product yields/C-mol % ^d													C _{bal} /%	[Pt] ppm ^g
			GLU	GLU _{1,4}	GLA	GL _{1,4}	GL _{6,3}	GL _{1,4;6,3}	GLUU ^e	GLUU _{6,3}	GUL	GUL _{6,3}	other ^f	CO ₂			
1	20% O ₂ / 60 °C/ 40 mg	34.6	13.2	7.0	1.3	0.2	1.0	0.0	1.5	1.2	3.7	2.0	0.4	0.1	97	1.8	
2	20% O ₂ / 80 °C/ 40 mg	49.0	8.3	7.7	3.1	0.8	2.8	0.2	2.8	3.5	6.6	6.1	2.6	1.8	97	7.9	
3	20% O ₂ / 100 °C/ 40 mg	90.0	1.2	3.1	1.2	0.3	0.9	0.8	1.3	4.6	5.5	7.5	4.2	2.2	43	34.8	
4	100% O ₂ / 60 °C/ 40 mg	43.1	15.7	9.7	2.0	0.4	1.9	0.	2.4	1.4	5.0	2.5	3.4	0.3	102	3.5	
5	100% O ₂ / 80 °C/ 40 mg	59.5	12.4	10.2	3.8	1.6	4.1	0.5	3.3	5.0	7.1	8.2	3.1	0.3	100	11.3	
6	100% O ₂ / 100 °C/ 40 mg	89.8	3.0	2.9	5.1	2.0	5.3	0.6	2.3	5.3	4.5	4.2	7.1	2.6	55	48.8	
7	100% O ₂ / 80 °C/ 80 mg	90.6	5.2	4.4	3.4	0.8	2.3	0.2	1.0	2.1	9.9	3.3	2.9	0.8	43	27.4	
8	20% O ₂ / 60 °C/ 40 mg	41.6	18.4	11.3	1.4	0.3	1.2	0.1	1.0	0.9	4.7	1.3	0.7	0.1	100	0.4	
9	20% O ₂ / 80 °C/ 40 mg	44.3	14.9	12.6	2.2	0.6	2.5	0.1	1.4	1.9	5.1	3.8	1.1	0.2	102	1.0	
10	20% O ₂ / 100 °C/ 40 mg	69.8	9.9	10.5	5.2	1.3	5.0	0.9	2.1	3.9	5.6	6.4	2.9	1.1	85	11.6	
11	100% O ₂ / 60 °C/ 40 mg	44.4	20.1	14.3	1.0	0.1	0.5	0.1	0.6	0.7	3.4	1.6	0.4	0.1	98	0.1	
12	100% O ₂ / 80 °C/ 40 mg	57.9	18.5	16.6	2.3	0.6	2.5	0.4	1.6	1.7	6.0	4.6	1.7	0.3	99	1.1	
13	100% O ₂ / 100 °C/ 40 mg	90.7	6.8	7.2	3.3	1.0	2.4	0.8	0.7	1.5	2.1	4.3	4.8	1.1	45	10.0	
14	100% O ₂ / 80 °C/ 80 mg	82.7	17.8	15.8	9.2	3.2	8.2	0.9	2.7	2.3	10.0	7.1	3.0	0.5	98	2.3	
15	100% O ₂ /100 °C/ 80 mg	99.5	3.2	3.6	4.2	1.2	3.4	1.9	0.1	0.7	2.0	2.4	5.4	2.8	31	12.4	
16	100% O ₂ / 100 °C/ 80 mg +80 mg XC72R ^h	98.2	4.1	4.1	16.7	6.2	14.9	2.6	0.5	1.0	4.0	3.6	8.4	2.9	71	5.2	
17	100% O ₂ / 100 °C/ 80 mg+ 160 mg XC72R ^h	98.4	4.1	4.1	23.8	7.5	23.0	6.0	0.6	0.7	3.7	3.3	11.5	2.8	93	1.4	

^aGLU (D-gluconic acid), GLU_{1,4} (D-glucono-1,4-lactone), GLA (D-glucaric acid), GL_{1,4} (D-glucaro-1,4-lactone), GL_{6,3} (D-glucaro-6,3-lactone), GL_{1,4,6,3} (D-glucaro-1,4,6,3-dilactone), GLUU (D-glucuronic acid), GLUU_{6,3} (D-glucurono-6,3-lactone), GUL (L-guluronic acid), GUL_{6,3} (L-gulurono 6,3-lactone). ^bGeneral conditions: [D-glucose] = 0.554 M (5.54 mmol in D₂O), 1000 rpm, *P*_{total} (X% O₂/ N₂) = 25 bar, 24 h. Entries 1–7; 5% Pt/TiO₂^{IMPRed400}, Entries 8–17; 5% Pt/C^{IMPRed400}. ^cGlucose conversion quantified from disappearance of glucose (α & β glucopyranose) using HMBC NMR. ^dAs CMB deviated from 100% under certain conditions, data presented as yield in C-mol %. ^eQuantified as α - and β -D-glucuronic acid. ^fOther (tartaric acid, tartronic acid, glycolic acid, glyceric acid, oxalic acid, acetic acid). ^gDetermined by MPAES (note: where 40 and 80 mg catalyst were used, 100% Pt leaching would afford a [Pt] of 200 and 400 ppm respectively). ^hReactor charged with carbon XC72R at *t* = 0.

Inc. recently patented the synthetic procedure for a series of shaped porous carbons,^{55–57} further still, that the examples in said patents featured use of the synthesized carbons as supports for Pt-based glucose oxidation catalysts.^{55–57} To further study the complex reaction pathways in operation in Pt-catalyzed glucose oxidation, a time on line study of the catalytic performance of 5% Pt/TiO₂^{IMPRed400} was carried out, and data are shown in Figure 2.

D-Gluconic acid (8) and D-glucono-1,4-lactone (9) are apparent primary products (Figure 2a), with their total selectivity decreasing from 70.7% at 2 h on line (χ = 19%) to 24.8% at 40 h (χ = 65%). Selectivity to L-guluronic acid (11) and the derived lactone L-gulurono-6,3-lactone (12) increases, consistent with their forming through dehydrogenation of D-gluconic acid (8). Selectivity toward D-glucuronic acids (4) and D-glucurono-6,3-lactone (6) also increases with increasing time on line, which suggests that this competing reaction pathway (Scheme 3) becomes more favorable at low pH. This is a minor pathway, however, with formation of D-gluconic acid favored. This is consistent with more facile

oxidation of D-glucose (1) at the terminal RCHO functional group than at the RCH₂OH. Selectivity toward D-glucaric acid and its derivatives also increases with increasing glucose conversion, with comparable selectivity toward D-glucaric acid (13) and D-glucaro-6,3-lactone (15) observed across 40 h on line (Figure 2c). Given the coelution of products shown in Figure S1, it should be noted that, had product streams from Figure 2 been analyzed by HPLC, it would not have been possible to distinguish between key major products, for example, D-gluconic acid (8) and D-glucaro-6,3-lactone (15). Indeed, while lactone products have never been reported in the catalytic D-glucose oxidation literature, C₆ lactones accounted for 45 ± 2.0% of all products represented across the 40 h time period in Figure 2. Consistent with Scheme 3, D-glucaric acid and its derivatives are the terminal C₆ oxidation products, and C–C scission yields increasing selectivity toward < C₆ products (Figure 2d and c). Indeed, total selectivity toward < C₆ products (tartaric, tartronic, oxalic, glycolic, glyceric, and acetic acids in addition to CO₂) reached 12.8% at 40 h on line (Figure 2e). For selectivity toward the total oxidation product,

CO₂ reached 4.1% at $\chi = 65\%$ (1.96% yield) based on observed products. A decrease in specific activity was observed with increasing time on line (Figure S13b), suggesting either competitive adsorption of reaction products or the onset of mass transport limitations at high degrees of either D-glucose or O₂ conversion. Indeed, using the CO chemisorption-determined Pt-surface site density ($4.43 \text{ m}^2_{\text{Pt}} \text{ g}_{\text{cat}}^{-1}$), the TOF of 5% Pt/TiO₂^{IMPRed400} at 2 h online was calculated as $144 \text{ mol}_{\text{Glucose-converted}} \text{ mol}_{\text{SurfacePt-sites}}^{-1} \text{ h}^{-1}$. This decreased to $25 \text{ mol}_{\text{Glucose-converted}} \text{ mol}_{\text{SurfacePt-sites}}^{-1} \text{ h}^{-1}$, averaged at $t = 39 \text{ h}$. Up to 24 h online ($\chi = 49.0\%$), the average observed carbon mass balance (CMB) was $98\% \pm 2$, but this fell to 83% at 40 h online ($\chi = 65\%$; Figure 2f). This decrease in CMB might be attributed to formation of insoluble humins, a process which is favorable under acidic conditions and elevated temperatures.⁵⁸ To confirm this, 5% Pt/TiO₂^{IMPRed400} was assessed across a temperature range of 60–100 °C (Table 2, entries 1–3).

Glucose conversion, measured at 24 h online, increased from 34.6% at a reaction temperature of 60 °C to 49.0% at 80 °C. Consistent with conversion selectivity relationships shown in Figure 2a–d, this increase in conversion was coupled with decreased selectivity toward primary products: D-gluconic acid/D-glucono-1,4-lactone, with increased selectivity toward D-glucuronic acid, L-guluronic acid, D-glucaric acid, lactone derivatives thereof, and < C₆ products. At a reaction temperature of 100 °C (25 bar of 20% O₂/N₂), the system became anaerobic ($\chi_{\text{glucose}} = 90.0\%$, 4.98 mmol glucose converted) with a 1:1 stoichiometry of converted glucose/O₂ in the charge gas (5.05 mmol O₂) of 1:1. The apparent CMB fell to 43% under these conditions (Table 2, entry 3). In the absence of O₂, formation of L-gulurono products (GUL/GUL_{6,3}) continued. Indeed, L-guluronic acid and its lactone derivative accounted for 40% of observed products (Table 2, entry 3). This is consistent with previous observations shown in Table S4, which further indicates that conversion of D-gluconic acid to D-glucaric acid proceeds via L-guluronic acid and, furthermore, that this proceeds via dehydrogenation of D-gluconic acid with zero order dependence with respect to PO₂. In the absence of O₂, oxidation of L-guluronic acid to yield D-glucaric (13) was prevented, with the total yield of D-glucaric acid and lactone derivatives thereof, falling to 3.2% (c.f., 6.9% at 80 °C Table 2, entries 2 and 3). This represents a potential chemocatalytic route toward the selective synthesis of L-guluronic acid, the monomer which affords rigidity in alginate biopolymers which have proven biomedical applications.^{59–61} L-Guluronic acid is currently produced commercially by hydrolysis of alginic acid, yielding the monomers L-guluronic acid (11) and D-mannuronic acid.

Analysis of the liquid and gaseous products streams of reactions represented in Table 2, entries 1–7, with low apparent CMBs showed no unidentified byproducts. To determine the fate of the missing carbon, the solid residue for reactions in Table 2, entries 1–3, representing a CMB range of 97–43%, was recovered by filtration, washed (100 mL H₂O), and dried (16 h, 110 °C) prior to thermogravimetric analysis (TGA; 5 °C min^{−1}, 20 mL min^{−1} air, 800 °C). Despite showing markedly different CMBs, no significant difference in mass loss was observed, suggesting that insoluble humin products or other carbonaceous species did not form under reaction conditions (Figure S16). Spectroscopic, chromatographic, and thermogravimetric analyses therefore offered no explanation as to the fate of the −57% CMB deficit in Table 2, entry 3. In a parametric study of 5% Pt/TiO₂^{IMPRed400} catalyzed

D-glucose oxidation (Table 2, entries 1–7), isoconversion of $90.1\% \pm 0.4$ was observed under three different reaction conditions (Table 2, entries 3, 6, and 7). Under these conditions, the observed CMB was <50% and significant Pt leaching was observed, exceeding 24% of total supported Pt (Table 2, entry 6).

It is well-known that the intensity of ¹H NMR resonance peaks is directly proportional to the population of ¹H. Indeed, that is the basis of quantitative ¹H NMR techniques. The intensity of HMBC NMR correlation peaks, however, is determined by through-bond coupling of two different spin active nuclei: ¹³C–¹H. At 100 °C, $P(\text{O}_2) = 5 \text{ bar}$, a significant concentration of Pt was leached into solution (34.8 ppm, Table 2, entry 3). This equated to leaching of ca. 17% of supported Pt. Low CMB reactions in Table 2 also correlated well with formation of orange product solutions, which is consistent with observations by Dirx et al. Sugar acids are effective chelating agents; indeed this an established commercial application for D-glucaric acid,^{27,36,62} and a general transfer of electron density occurs when an organic acid chelates a cationic metal center. This might be expected to effect changes in absolute areas of ¹H–¹³C through bond couplings. The role of leached Pt in effecting low CMBs was confirmed through analysis of combined data from Tables 1 and 2 and Figure 2.

For all Pt catalysts, increasing D-glucose conversion correlated well with decreasing CMB (Figure 3a) and increasing Pt leaching (Figure 3b). When the [Pt] remaining in solution postreaction exceeded 10 ppm, a rapid decrease in CMB was observed (Figure 3c). In general, 5% Pt/C catalysts showed lower [Pt] at isoconversion than did SiO₂- and TiO₂-supported analogues (Figure 3b), which is consistent with the ability of carbon to sequester leached Pt from solution, as shown in Figure S14. To confirm the role of leached metal species in effecting decreased CMBs, 5% Pt/C^{IMPRed400} was assessed under high conversion conditions with an increasing mass of XC72R (0–160 mg) added at $t = 0$ to promote sequestration of metals from solution (Table 2, entries 15–17). Isoconversion of glucose was observed across these conditions ($98.7 \pm 0.7\%$). The addition of 160 mg of carbon led to decreased [Pt] (12.4–1.4 ppm) and increased observed CMB (31–93%; Table 2, entries 15 and 17). The total yield of C₆ lactones in Table 2, entry 17, was 43.6%. HMBC NMR quantification of D-glucaric acid and D-tartaric acid, both well-known chelating agents, suffered significantly in the presence of leached cations. Indeed, the observed D-glucaro (GLA, GL_{1,4}, GL_{6,3}, and GL_{1,4;6,3})/D-tartaric acid yields increased from 8.8%/2.3% to 60.3%/8.4% when 160 mg of carbon XC72 R was added to the reactor. The average mass-normalized D-glucaro (GLA, GL_{1,4}, GL_{6,3}, GL_{1,4;6,3}) productivity across 24 h online for data in Table 2 entry 17 was $1.71 \text{ mol}_{\text{D-glucarates}} \text{ kg}_{\text{cat}}^{-1} \text{ h}^{-1}$. This compares favorably with the optimal D-glucaric acid synthesis rate previously reported by Boussie et al. for a 4% Pt/SiO₂ catalyst ($1.42 \text{ mol}_{\text{D-glucaric acid}} \text{ kg}_{\text{cat}}^{-1} \text{ h}^{-1}$; 8 h, 90 °C, $P_{\text{O}_2} = 5 \text{ bar}$, Pt/glucose = 1:84 mol/mol). Dirx et al. previously reported increased rates of D-glucaric acid formation over Pt catalysts when the reaction pH was maintained at pH 9–10 through autotitration of NaOH_{aq}.^{27,39} This was attributed to more efficient desorption of acid products from the catalyst surface under basic conditions.^{27,39} Such decreased contact times could decrease product-mediated chemical leaching and therefore [Pt]. Unfortunately, the addition of NaOH (1 equiv) at $t = 0$ caused a significant decrease in the resolution of

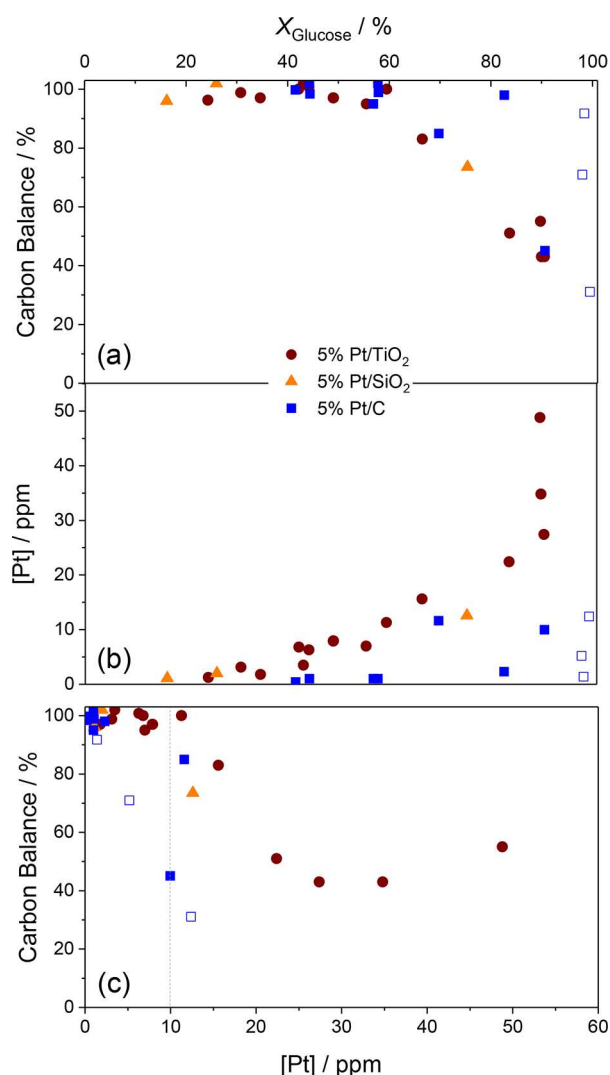


Figure 3. Interdependency between X_{Glucose} , observed CMB, and $[\text{Pt}]$ showing data from Tables 1 and 2 and Figure 2. Blue ■, 5% Pt/C; orange ▲, 5% Pt/SiO₂; and red ●, 5% Pt/TiO₂ catalysts prepared by CVI, IMP, and IWI (blue □, 5% Pt/C^{IMPRed400} from Table 2, entries 15–17).

HMBC NMR spectra (Figure S17). As a result, it was not possible to quantify either D-glucose conversion or formation of products under such pH-controlled conditions.

It is clear from Figure 3a and b that the addition of increasing masses of carbon (XC72R) significantly decreased observed $[\text{Pt}]$ and consequently led to increased CMB. To avoid introduction of mass transport limitation effects, the carbon additive charge was limited to ≤ 160 mg in the 10 mL reaction. Extrapolation of data in Table 2, entries 15–17, suggests that further addition of carbon would yield a metal-free product stream and closed CMB. On the basis of trends in closed batch (Figure 3b) and trickle flow regimes (Figure S15), it is therefore clear that operation in continuous flow would be favorable on scale-up. Use of a Pt/C catalyst with downstream high purity carbon beds, might be expected to afford product streams rich in D-glucaric acid or its lactone derivatives, with leached metal sequestered and thereby recoverable. Development of such a process will be addressed in a future study.

3. CONCLUSIONS

For the first time, quantitative 2D HMBC NMR has been applied in both determining and quantifying the products of chemocatalytic reactions. Linear, first order calibrations, use of a self-contained TMS standard, and sensitivity analyses remove degrees of uncertainty encountered in previous attempts to employ 2D NMR as a quantitative tool for analysis of complex mixtures. The developed analytical technique was then employed in identifying and quantifying the myriad C₆ products, both carboxylic acids and lactones, which form spontaneously during non-pH controlled aerobic oxidation of D-glucose over heterogeneous Pt catalysts. For the first time, CO₂ has been quantified as a product of this oft studied reaction, with not-insignificant yields of up to 2.9% observed. The reaction pathway is more complex than has previously been reported, with C₆ five-membered lactone products accounting for ca. 45% of all products observed over 40 h on line. All lactonizations proceed with retention of stereochemistry at the secondary alcohol center, that is, by activation of the carboxylic acid, followed by nucleophilic attack by said alcohol (hydroxyl) and loss of a hydroxyl from the acid. Two primary uronic acid products form, D-glucuronic acid (4) and D-gluconic acid (8). These both establish equilibria with their -6,3- (6) and -1,4- (9) lactones, respectively. While D-glucuronic acid and its lactone undergo direct oxidation to yield D-glucaric acid (13), D-gluconic acid and its derivative lactone are shown to undergo dehydrogenation to yield L-guluronic acid (11), which rapidly dehydrates to form L-gulurono-6,3-lactone (12). Oxidation of L-guluronic acid and its lactone leads to the desired product of Pt-catalyzed D-glucose oxidation, D-glucaric acid (13). Equilibration of D-glucaric acid to D-glucaro-1,4-lactone (14), D-glucaro-6,3-lactone (15), and D-glucaro-1,4:6,3-dilactone (16) is then observable and quantifiable via HMBC NMR, with D-glucaro-6,3-lactone yields often equaling those of D-glucaric acid itself. Crucially, observation of D-glucaro lactones is not possible using chromatographic techniques used in all previous studies of this reaction; indeed, we attribute the low D-glucaric acid yields reported in many previous studies, to coelution of D-glucaro lactones with D-gluconic acid, which is normally reported to be both a primary and major reaction product. Extensive product-mediated leaching of the active phase –Pt is reported and attributed to chelation of oxidized Pt species by carboxylic acid products. A strong chelating effect was confirmed, with the ¹³C–¹H correlation peaks of D-glucaric acid shown to be significantly quenched by a $[\text{Pt}]$ of as low as 10 ppm. This was shown to impact significantly upon product quantification, with carbon mass balances of <50% observed. Catalyst design studies showed D-glucose conversion to increase proportional to the Pt surface area. Through supporting of Pt onto carbon black (XC72R) via a range of preparation techniques, catalysts can be synthesized which afford appreciable specific activities and product streams containing a low $[\text{Pt}]$. Rather than being due to enhanced stability toward leaching, the latter is attributed to carbon's affinity for adsorbing leached Pt *in situ*. Preliminary parametric optimization of reaction conditions employed in assessing 5% Pt/C prepared by IMP led to high D-glucose conversion (98.4%), relatively low $[\text{Pt}]$ in solution (1.4 ppm), and consequently high CMB (93%). Under said conditions, the total yield of previously unreported C₆ lactones was 43.6%, with 35.5% yield being D-glucaro lactone and dilactone

products. This work therefore lays the foundation for future studies into catalytic biomass-valorization, detailing a new approach to analysis of complex reaction mixtures and application thereof to provide vital insight as to the true pathways in operation during the Pt-catalyzed oxidation of D-glucose to D-glucaric acid. This should inform future kinetic studies of the competing pathways in operation during catalytic D-glucose oxidation as well as catalyst design/screening studies.

■ ASSOCIATED CONTENT

● Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.8b03838.

Detailed NMR spectral assignments, details pertaining to development of the quantitative HMBC protocol, data for product conversion reactions, plots showing specific catalyst activity, Pt-leaching/sequestration studies, and thermogravimetric analyses of catalysts prior to and following catalytic testing (PDF)

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Funding

This work was supported by the Engineering and Physical Sciences Research Council (EPSRC, UK (EP/K014749)).

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the Engineering and Physical Sciences Research Council EPSRC, UK (EP/K014749). Information on the data underpinning the results presented here, including how to access them, can be found in the Cardiff University data catalogue at <http://doi.org/10.17035/d.2018.0065256615>.

■ ABBREVIATIONS

HMBC, heteronuclear multiple bond correlation spectroscopy; NMR, nuclear magnetic resonance

■ REFERENCES

- (1) Abbadi, A.; van Bekkum, H. Effect of pH in the Pt-catalyzed oxidation of D-glucose to D-gluconic acid. *J. Mol. Catal. A: Chem.* **1995**, *97*, 111–118.
- (2) Biella, S.; Prati, L.; Rossi, M. Selective Oxidation of D-Glucose on Gold Catalyst. *J. Catal.* **2002**, *206*, 242–247.
- (3) Comotti, M.; Della Pina, C.; Matarrese, R.; Rossi, M. Heterogeneous catalysis: The catalytic activity of "Naked" gold particles. *Angew. Chem., Int. Ed.* **2004**, *43*, 5812–5815.
- (4) Despevroux, B. M.; Deller, K.; Peldszus, E. The use of precious metal catalysts supported on activated carbon in oxidation reactions for the synthesis of fine chemicals, especially for the selective oxidation of glucose to gluconic acid. *Stud. Surf. Sci. Catal.* **1990**, *55*, 159–168.
- (5) Miedziak, P. J.; Alshammari, H.; Kondrat, S. A.; Clarke, T. J.; Davies, T. E.; Morad, M.; Morgan, D. J.; Willock, D. J.; Knight, D. W.; Taylor, S. H.; Hutchings, G. J. Base-free glucose oxidation using air with supported gold catalysts. *Green Chem.* **2014**, *16*, 3132–3141.
- (6) Solmi, S.; Morreale, C.; Ospitali, F.; Agnoli, S.; Cavani, F. Oxidation of D-Glucose to Glucaric Acid Using Au/C Catalysts. *ChemCatChem* **2017**, *9*, 2797–2806.
- (7) Besson, M.; Flèche, G.; Fuertes, P.; Gallezot, P.; Lahmer, F. Oxidation of glucose and gluconate on Pt, Pt Bi, and Pt Au catalysts. *Recueil des Travaux Chimiques des Pays-Bas* **1996**, *115*, 217–221.
- (8) Besson, M.; Lahmer, F.; Gallezot, P.; Fuertes, P.; Fleche, G. Catalytic oxidation of glucose on bismuth-promoted palladium catalysts. *J. Catal.* **1995**, *152*, 116–121.
- (9) Wenkin, M.; Ruiz, P.; Delmon, B.; Devillers, M. The role of bismuth as promoter in Pd-Bi catalysts for the selective oxidation of glucose to gluconate. *J. Mol. Catal. A: Chem.* **2002**, *180*, 141–159.
- (10) Werpy, T.; Peterson, G. Top Value Added Chemicals From Biomass, Volume 1—Results of Screening for Potential Candidates from Sugars and Synthesis Gas; Energy Efficiency and Renewable Energy (EERE): <http://www.eere.energy.gov/biomass/pdfs/35523.pdf>, 2004.
- (11) Sohst, O.; Tollens, B. Über krystallisierte Zuckersäure (Zuckerlactonsäure). *Justus Liebigs Annalen der Chemie* **1888**, *245*, 1–27.
- (12) Mehlretter, C. L.; Rist, C. E. Saccharic and oxalic acids by the nitric acid oxidation of dextrose. *J. Agric. Food Chem.* **1953**, *1*, 779–83.
- (13) Smith, T. N.; Hash, K.; Davey, C. L.; Mills, H.; Williams, H.; Kiely, D. E. Modifications in the nitric acid oxidation of D-glucose. *Carbohydr. Res.* **2012**, *350*, 6–13.
- (14) Olas, B.; Saluk-Juszczak, J.; Wachowicz, B. D-glucaro 1,4-lactone and resveratrol as antioxidants in blood platelets. *Cell Biol. Toxicol.* **2008**, *24*, 189–199.
- (15) Saluk-Juszczak, J.; Olas, B.; Nowak, P.; Staroń, A.; Wachowicz, B. Protective effects of d-glucaro-1,4-lactone against oxidative modifications in blood platelets. *Nutr., Metab. Cardiovasc. Dis.* **2008**, *18*, 422–428.
- (16) Walaszek, Z. Potential use of D-glucaric acid derivatives in cancer prevention. *Cancer Lett. (N. Y., NY, U. S.)* **1990**, *54*, 1–8.
- (17) Walaszek, Z.; Szemraj, J.; Hanausek, M.; Adams, A. K.; Sherman, U. d-Glucaric acid content of various fruits and vegetables and cholesterol-lowering effects of dietary d-glucarate in the rat. *Nutr. Res. (N. Y., NY, U. S.)* **1996**, *16*, 673–681.
- (18) Chen, L.; Kiely, D. E. Synthesis of Stereoregular Head-Tail Hydroxylated Nylons Derived from D-Glucose. *J. Org. Chem.* **1996**, *61*, 5847–5851.
- (19) Archer, R.; Diamond, G. M.; Dias, E. L.; Murphy, V. J.; Petro, M.; Super, J. D. Processes for the production of adipic acid from D-glucose via hydro-deoxygenation and water concentration reduction in synthesis of hexamethylene diamine and caprolactam. WO2013090031A2, 2013.
- (20) Boussie, T. R.; Dias, E. L.; Fresco, Z. M.; Murphy, V. J.; Shoemaker, J.; Archer, R.; Jiang, H. Production of adipic acid and derivatives from carbohydrate-containing materials. WO2010144862A2, 2010.
- (21) Boussie, T. R.; Dias, E. L.; Fresco, Z. M.; Murphy, V. J.; Shoemaker, J.; Archer, R.; Jiang, H. Adipic acid production from carbohydrate-containing materials. US8669397B2, 2014.
- (22) Moon, T. S.; Yoon, S. H.; Lanza, A. M.; Roy-Mayhew, J. D.; Prather, K. L. Production of glucaric acid from a synthetic pathway in recombinant Escherichia coli. *Appl. Environ. Microbiol.* **2009**, *75*, 589–95.
- (23) Shiue, E.; Brockman, I. M.; Prather, K. L. J. Improving product yields on D-glucose in Escherichia coli via knockout of pgi and zwf and feeding of supplemental carbon sources. *Biotechnol. Bioeng.* **2015**, *112*, 579–587.
- (24) Shiue, E.; Prather, K. L. J. Improving D-glucaric acid production from myo-inositol in E. coli by increasing MIOX stability and myo-inositol transport. *Metab. Eng.* **2014**, *22*, 22–31.
- (25) Bin, D.; Wang, H.; Li, J.; Wang, H.; Yin, Z.; Kang, J.; He, B.; Li, Z. Controllable oxidation of glucose to gluconic acid and glucaric acid

using an electrocatalytic reactor. *Electrochim. Acta* **2014**, *130*, 170–178.

(26) Ibert, M.; Fuertes, P.; Merbouh, N.; Fiol-Petit, C.; Feasson, C.; Marsais, F. Improved preparative electrochemical oxidation of D-glucose to D-glucaric acid. *Electrochim. Acta* **2010**, *55*, 3589–3594.

(27) Dirkx, J. M. H.; van der Baan, H. S.; van den Broen, J. M. A. J. J. The preparation of D-glucaric acid by the oxidation of D-gluconic acid catalysed by platinum on carbon. *Carbohydr. Res.* **1977**, *59*, 63–72.

(28) Dirkx, J. M. H.; van der Baan, H. S. The oxidation of glucose with platinum on carbon as catalyst. *J. Catal.* **1981**, *67*, 1–13.

(29) Murphy, V. J.; Shoemaker, J.; Zhu, G.; Archer, R.; Salem, G. F.; Dias, E. L. Oxidation catalysts for oxidative chemocatalytic conversion of carbohydrates to carboxylic acids or their derivatives. US20110306790A1, 2011.

(30) Boussie, T. R.; Dias, E. L.; Fresco, Z. M.; Murphy, V. J.; Shoemaker, J.; Archer, R.; Jiang, H. Adipic acid-containing compositions for production of monomers and polymers. US20110218318A1, 2011.

(31) Derrien, E.; Marion, P.; Pinel, C.; Besson, M. Influence of Residues Contained in Softwood Hemicellulose Hydrolysates on the Catalytic Oxidation of Glucose to Glucarate in Alkaline Aqueous Solution. *Org. Process Res. Dev.* **2016**, *20*, 1265–1275.

(32) Jin, X.; Zhao, M.; Vora, M.; Shen, J.; Zeng, C.; Yan, W.; Thapa, P. S.; Subramaniam, B.; Chaudhari, R. V. Synergistic Effects of Bimetallic PtPd/TiO₂ Nanocatalysts in Oxidation of Glucose to Glucaric Acid: Structure Dependent Activity and Selectivity. *Ind. Eng. Chem. Res.* **2016**, *55*, 2932–2945.

(33) Lee, J.; Saha, B.; Vlachos, D. G. Pt catalysts for efficient aerobic oxidation of glucose to glucaric acid in water. *Green Chem.* **2016**, *18*, 3815.

(34) Thaburet, J.-F.; Merbouh, N.; Ibert, M.; Marsais, F.; Queguiner, G. TEMPO-mediated oxidation of maltodextrins and D-glucose: effect of pH on the selectivity and sequestering ability of the resulting polycarboxylates. *Carbohydr. Res.* **2001**, *330*, 21–29.

(35) Jin, X.; Zhao, M.; Shen, J.; Yan, W.; He, L.; Thapa, P. S.; Ren, S.; Subramaniam, B.; Chaudhari, R. V. Exceptional performance of bimetallic Pt1Cu3/TiO₂ nanocatalysts for oxidation of gluconic acid and glucose with O₂ to glucaric acid. *J. Catal.* **2015**, *330*, 323–329.

(36) Lin, H.; Su, J.; Liu, Y.; Yang, L. Catalytic Conversion of Lignocellulosic Biomass to Value-Added Organic Acids in Aqueous Media. In *Application of Hydrothermal Reactions to Biomass Conversion*; Jin, F., Ed.; Springer: Berlin, 2014; pp 109–138.

(37) Karski, S.; Paryczak, T.; Witonska, I. Selective Oxidation of Glucose to Gluconic Acid over Bimetallic Pd-Me Catalysts (Me = Bi, Tl, Sn, Co). *Kinet. Catal.* **2003**, *44*, 618–622.

(38) Archer, R.; Diamond, G. M.; Dias, E. L.; Murphy, V. J.; Petro, M.; Super, J. D. Process for the separation of mono- and di-carboxylic acid compounds. WO2013090032A1, 2013.

(39) Dirkx, J. M. H.; van der Baan, H. S. The oxidation of gluconic acid with platinum on carbon as catalyst. *J. Catal.* **1981**, *67*, 14–20.

(40) Brown, J. M.; Manley-Harris, M.; Field, R. J.; Kiely, D. E. An NMR study of the equilibration of D-glucaric acid with lactone forms in aqueous acid solutions. *J. Carbohydr. Chem.* **2007**, *26*, 455–467.

(41) Giraudeau, P. Quantitative 2D liquid-state NMR. *Magn. Reson. Chem.* **2014**, *52*, 259–272.

(42) Martineau, E.; El Khantache, K.; Pupier, M.; Sepulcri, P.; Akoka, S.; Giraudeau, P. Non-linear effects in quantitative 2D NMR of polysaccharides: Pitfalls and how to avoid them. *J. Pharm. Biomed. Anal.* **2015**, *108*, 78–85.

(43) Armstrong, R. D.; Kariuki, B. M.; Knight, D. W.; Hutchings, G. J. How to Synthesise High Purity, Crystalline d-Glucaric Acid Selectively. *Eur. J. Org. Chem.* **2017**, *2017*, 6811–6814.

(44) Archer, R.; Diamond, G. M.; Dias, E. L.; Murphy, V. J.; Petro, M.; Super, J. D. Processes for the production of adipic acid from D-glucose via hydro-deoxygenation and water concentration reduction in synthesis of hexamethylene diamine and caprolactam. WO2013090031A2, 2013.

(45) Rautiainen, S.; Lehtinen, P.; Chen, J.; Vehkamäki, M.; Niemela, K.; Leskela, M.; Repo, T. Selective oxidation of uronic acids into aldaric acids over gold catalyst. *RSC Adv.* **2015**, *5*, 19502–19507.

(46) Horton, D.; Walaszek, Z.; Ekiel, I. Conformations of d-gluconic, d-mannonic, and d-galactonic acids in solution, as determined by n.m.r. spectroscopy. *Carbohydr. Res.* **1983**, *119*, 263–268.

(47) Wang, Z.-T.; Hoyt, R. A.; El-Soda, M.; Madix, R. J.; Kaxiras, E.; Sykes, E. C. H. Dry Dehydrogenation of Ethanol on Pt–Cu Single Atom Alloys. *Top. Catal.* **2018**, *61*, 328–335.

(48) Shan, J.; Janvelyan, N.; Li, H.; Liu, J.; Egle, T. M.; Ye, J.; Biener, M. M.; Biener, J.; Friend, C. M.; Flytzani-Stephanopoulos, M. Selective non-oxidative dehydrogenation of ethanol to acetaldehyde and hydrogen on highly dilute NiCu alloys. *Appl. Catal., B* **2017**, *205*, 541–550.

(49) Forde, M. M.; Armstrong, R. D.; Hammond, C.; He, Q.; Jenkins, R. L.; Kondrat, S. A.; Dimitratos, N.; Lopez-Sanchez, J. A.; Taylor, S. H.; Willock, D.; Kiely, C. J.; Hutchings, G. J. Partial Oxidation of Ethane to Oxygenates Using Fe- and Cu-Containing ZSM-5. *J. Am. Chem. Soc.* **2013**, *135*, 11087–11099.

(50) Nowicka, E.; Sankar, M.; Jenkins, R. L.; Knight, D. W.; Willock, D. J.; Hutchings, G. J.; Francisco, M.; Taylor, S. H. Selective Oxidation of Alkyl-Substituted Polyaromatics Using Ruthenium-Ion-Catalyzed Oxidation. *Chem. - Eur. J.* **2015**, *21*, 4285–4293.

(51) Her, C.; Alonzo, A. P.; Vang, J. Y.; Torres, E.; Krishnan, V. V. Real-Time Enzyme Kinetics by Quantitative NMR Spectroscopy and Determination of the Michaelis–Menten Constant Using the Lambert-W Function. *J. Chem. Educ.* **2015**, *92*, 1943–1948.

(52) Singh, J.; Her, C.; Krishnan, V. V. Enzymatic conversion of sucrose to glucose and its anomerization by quantitative NMR spectroscopy: Application of a simple consecutive reaction rates approach. *J. Mol. Struct.* **2018**, *1153*, 187–191.

(53) Wang, X. L.; Liu, W.; Yu, Y.-Y.; Song, Y.; Fang, W. Q.; Wei, D.; Gong, X.-Q.; Yao, Y.-F.; Yang, H. G. Operando NMR spectroscopic analysis of proton transfer in heterogeneous photocatalytic reactions. *Nat. Commun.* **2016**, *7*, 11918.

(54) Hammond, C.; Forde, M. M.; Ab Rahim, M. H.; Thetford, A.; He, Q.; Jenkins, R. L.; Dimitratos, N.; Lopez-Sanchez, J. A.; Dummer, N. F.; Murphy, D. M.; Carley, A. F.; Taylor, S. H.; Willock, D. J.; Stangland, E. E.; Kang, J.; Hagen, H.; Kiely, C. J.; Hutchings, G. J. Direct Catalytic Conversion of Methane to Methanol in an Aqueous Medium by using Copper-Promoted Fe-ZSM-5. *Angew. Chem., Int. Ed.* **2012**, *51*, 5129–5133.

(55) Dias, E. L.; Hagemeyer, A.; Jiang, H. X.; Longmire, J.; Shoemaker, J. A. W.; Sokolovskii, V.; Zhu, G.; Murphy, V. J.; Diamond, G. M. Carbon black based shaped porous products. WO2015168327A1, 2015.

(56) Diamond, G. M.; Zhu, G.; Murphy, V. J.; Dias, E. L. Porous shaped carbon products. WO2017075391A1, 2017.

(57) Sokolovskii, V.; Hagemeyer, A.; Shoemaker, J. A. W.; Guerbuez, E. I.; Zhu, G.; Dias, E. L. Porous shaped metal-carbon products. US20170120223A1, 2017.

(58) Patil, S. K. R.; Heltzel, J.; Lund, C. R. F. Comparison of Structural Features of Humins Formed Catalytically from Glucose, Fructose, and 5-Hydroxymethylfurfuraldehyde. *Energy Fuels* **2012**, *26*, 5281–5293.

(59) Muri, J. M.; Brown, P. J. Alginate fibers A2 - Blackburn, R.S. In *Biodegradable and Sustainable Fibres*, 1st ed.; Woodhead Publishing: Cambridge, 2005; pp 89–110.

(60) Ivanova, E. P.; Bazaka, K.; Crawford, R. J. Natural polymer biomaterials: advanced applications. In *New Functional Biomaterials for Medicine and Healthcare*, 1st ed.; Woodhead Publishing: Cambridge, 2014; pp 32–70.

(61) Rajendran, S.; Anand, S. C.; Rigby, A. J. Textiles for healthcare and medical applications. In *Handbook of Technical Textiles*, 2nd ed.; Woodhead Publishing: Cambridge, 2016; pp 135–168.

(62) Fischer, K.; Bipp, H.-P. Removal of Heavy Metals from Soil Components and Soils by Natural Chelating Agents. Part II. Soil Extraction by Sugar Acids. *Water, Air, Soil Pollut.* **2002**, *138*, 271–288.